PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
CDJ-346PC		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2008/082745	07/11/2008	07/11/2007
Applicant		
CELLDEX THERAPEUTICS INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 8 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**

☒ the text is approved as submitted by the applicant

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant

☐ as selected by this Authority, because the applicant failed to suggest a figure

☐ as selected by this Authority, because this figure better characterizes the invention

b. ☒ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/082745

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] on paper

   [X] in electronic form

   c. time of filing/furnishing

   [X] contained in the international application as filed

   [X] filed together with the international application in electronic form

   [ ] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/082745

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/395 A61P35/00 C07K16/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61P C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/035619 A (CENTENARY INST CANCER MEDICINE [AU]; BRITTON WARWICK [AU]; DEMANGEL CA) 29 April 2004 (2004-04-29) page 40 - page 48 figure 3A ----- -/--	1-4,6-84

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 January 2009	08/07/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Cilensek, Zoran

3

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BADIEE ET AL: "Enhanced delivery of immunoliposomes to human dendritic cells by targeting the multilectin receptor DEC-205" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 25, no. 25, 30 May 2007 (2007-05-30), pages 4757-4766, XP022098619 ISSN: 0264-410X figures 3-6 page 4758, right-hand column, paragraph 4 - page 4759, left-hand column, paragraph 1 page 4761 page 4765, left-hand column, paragraph 3 - right-hand column, paragraph 2	1-4,6-84
X	GUO M ET AL: "A monoclonal antibody to the DEC-205 endocytosis receptor on human dendritic cells" HUMAN IMMUNOLOGY, NEW YORK, NY, US, vol. 61, no. 8, 1 August 2000 (2000-08-01), pages 729-738, XP002319045 ISSN: 0198-8859 page 730, right-hand column, paragraph 2 page 732, right-hand column, paragraph 2 figures 2,4-6	1-4,6-84
X	US 2005/186612 A1 (HART DEREK N [NZ]) 25 August 2005 (2005-08-25) paragraph [0114] figure 9	1-4,6-84
X	WO 2004/074432 A (MEDAREX INC [US]; KELER TIBOR [US]; ENDRES MICHAEL [US]; HE LIZHEN [US]) 2 September 2004 (2004-09-02) page 34, line 16 - page 39, line 17 figures 9,14	1-4,6-84
A	WO 2005/018610 A (LIPOTEK PTY LTD [AU]; ALTIN JOSEPH [AU]; PARISH CHRISTOPHER RICHARD [A) 3 March 2005 (2005-03-03) page 20, line 15 - page 23, line 20	1-4,6-84
A	US 2004/258688 A1 (HAWIGER DANIEL [US] ET AL) 23 December 2004 (2004-12-23) paragraphs [0356], [0378] - [0389] figures 10-12	1-4,6-84

3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/082745

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

15, 24 and 28 (all fully), 1-4, 6-14, 16-23
25-27 and 29-84 (all partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 15, 24, and 28 (all fully), 1-4,6-14,16-23,25-27 and 29-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises heavy and light chain variable region CDR1, CDR2 and CDR3 sequences selected from the group consisting of a heavy chain variable region CDR1 comprising SEQ ID NO.29, a heavy chain variable region CDR2 comprising SEQ ID NO.30, a heavy chain variable region CDR3 comprising SEQ ID NO.31, a light chain variable region CDR1 comprising SEQ ID NO.35, a light chain variable region CDR2 comprising SEQ ID NO.36, and a light chain variable region CDR3 comprising SEQ ID NO.37. An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy and light chain variable region comprising SEQ ID NOs: 28 and 34 respectively.

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2. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:5-7 and 11-13 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 4 and 10 respectively.

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3. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:17-19 and 23-25 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 16 and 22 respectively.

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4. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:41-43 and 47-49 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 40 and 46 respectively.

---

5. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:53-55 and 59-61 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 52 and 58 respectively.

---

6. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:77-79 and 83-85 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 76 and 82 respectively.

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7. claims: 1-4,6-9,12,13,16,21,25,29,31-33,35-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 88.

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8. claims: 1-3,5-9,12,13,16,21,25,29,31-33,35-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 64.

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9. claims: 1-3,5-9,12,13,16,21,25,29,31-33,35-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 70.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/082745

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004035619 A	29-04-2004	AU 2003271430 A1	04-05-2004
US 2005186612 A1	25-08-2005	NONE	
WO 2004074432 A	02-09-2004	AU 2004213749 A1	02-09-2004
		CA 2514979 A1	02-09-2004
		CN 1767852 A	03-05-2006
		EP 1594533 A2	16-11-2005
		JP 2006516637 T	06-07-2006
		NZ 541903 A	29-08-2008
		ZA 200506202 A	25-10-2006
WO 2005018610 A	03-03-2005	CN 1893925 A	10-01-2007
		EP 1660040 A1	31-05-2006
		JP 2007502780 T	15-02-2007
		US 2007026057 A1	01-02-2007
US 2004258688 A1	23-12-2004	NONE	

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2008/082745	07.11.2008	07.11.2007

International Patent Classification (IPC) or both national classification and IPC
INV. A61K39/395 A61P35/00 C07K16/28

Applicant
CELLDEX THERAPEUTICS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Cilensek, Zoran Telephone No. +49 89 2399-8207

Form PCT/ISA/237 (Cover Sheet) (April 2005)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☒ on paper

      ☒ in electronic form

   c. time of filing/furnishing:

      ☒ contained in the international application as filed.

      ☒ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 5 (fully) and 1-4, 6-84 (parts with respect to Inventions 2-9)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 5 (fully) and 1-4, 6-84 (with respect to Inventions 2-9)

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 15, 24 and 28 (all fully) and 1-4, 6-14, 16-23, 25-27 and 29-84 (all partially)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4,6-15,17-84
	No:	Claims	16
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-4,6-84
Industrial applicability (IA)	Yes:	Claims	1-4,6-84
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: WO 2004/035619 A (CENTENARY INST CANCER MEDICINE [AU]; BRITTON WARWICK [AU]; DEMANGEL CA) 29 April 2004 (2004-04-29)

D2: BADIEE ET AL: "Enhanced delivery of immunoliposomes to human dendritic cells by targeting the multilectin receptor DEC-205" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 25, no. 25, 30 May 2007 (2007-05-30), pages 4757-4766, XP022098619 ISSN: 0264-410X

D3: GUO M ET AL: "A monoclonal antibody to the DEC-205 endocytosis receptor on human dendritic cells" HUMAN IMMUNOLOGY, NEW YORK, NY, US, vol. 61, no. 8, 1 August 2000 (2000-08-01), pages 729-738, XP002319045 ISSN: 0198-8859

D4: US 2005/186612 A1 (HART DEREK N [NZ]) 25 August 2005 (2005-08-25)

D5: WO 2004/074432 A (MEDAREX INC [US]; KELER TIBOR [US]; ENDRES MICHAEL [US]; HE LIZHEN [US) 2 September 2004 (2004-09-02)

D6: WO 2005/018610 A (LIPOTEK PTY LTD [AU]; ALTIN JOSEPH [AU]; PARISH CHRISTOPHER RICHARD [A) 3 March 2005 (2005-03-03)

Re Item IV

1 Lack of unity of invention

1.1 The underlying application relates to antibodies to human DEC205. Such antibodies are known in the art. For instance, D1 discloses the sequence of a rat anti DEC205 monoclonal antibody termed NLDC-145 (ATCC Accession No. HB-2990), wherein the variable heavy chain CDR3 sequence RYFDL falls in the consensus (core) variable heavy chain CDR3 of the antibodies of the underlying application (compare D1, Figure 3A with Figure 6 of the underlying application). D3 discloses the production of a murine monoclonal antibody termed MG38 against the cysteine-rich and fibronectin II domain of human DEC205, wherein the antibody does not recognize murine DEC205 (page 730, righthand column, §2, page 732, righthand column, §2 and Figures 2,4,5 and 6). D4 discloses monoclonal antibodies raised in mice to two peptides derived from the human DEC205 sequence (residues 1267-1277 and 1227-123), see § 114 and Figure 9. D5 discloses a fully human antibody termed B11 specific for the mannose receptor on dendritic cells, wherein the light chain variable region is identical to the antibody heavy chain 2F4 of the current

application (compare D5, Figures 9 and 14 with Figure 5 of the current application). The antibody was fused to the human chorionic gonadotropin antigen and the conjugate used to stimulate T cell responses (page 34, line 16-page 39, line 17).

1.2 In the light of the prior art, the problem to be solved may therefore be defined as the provision of further antibodies to human DEC205. The following solutions are provided in the claims:

1. An isolated monoclonal antibody which binds to human DEC205 and comprises heavy and light chain variable region CDR1, CDR2 and CDR3 sequences selected from the group consisting of a heavy chain variable region CDR1 comprising SEQ ID NO.29, a heavy chain variable region CDR2 comprising SEQ ID NO.30, a heavy chain variable region CDR3 comprising SEQ ID NO.31, a light chain variable region CDR1 comprising SEQ ID NO.35, a light chain variable region CDR2 comprising SEQ ID NO.36, and a light chain variable region CDR3 comprising SEQ ID NO.37. An isolated monoclonal antibody which binds to human DEC205 and comprises a heavy and light chain variable region comprising SEQ ID NOs: 28 and 34 respectively ((claims 15, 24, and 28 (all fully), 1-4,6-14,16-23,25-27 and 29-84 (all partially)).

2. Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:5-7 and 11-13 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 4 and 10 respectively.((claims 1-4,6-14,16-23,25-27 and 29-84 (all partially)).

3. Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:17-19 and 23-25 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 16 and 22 respectively (claims 1-4,6-14,16-23,25-27 and 29-84 (all partially)).

4. Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:41-43 and 47-49 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 40 and 46 respectively ((claims 1-4,6-14,16-23,25-27 and 29-84 (all partially)).

5. Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:53-55 and 59-61 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 52 and 58 respectively ((claims 1-4,6-14,16-23,25-27 and 29-84

(all partially)).

6. Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:77-79 and 83-85 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 76 and 82 respectively ((claims 1-4,6-14,16-23,25-27 and 29-84 (all partially)).

7. An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO:88 ((claims 1-4, 6-9,12,13,16,21,25,29,31-33,35-84 (all partially)).

8. An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 64 ((claims 1-3,5-9,12,13,16,21,25,29,31-33,35-84 (all partially)).

9. An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 70 ((claims 1-3,5-9,12,13,16,21,25,29,31-33,35-84 (all partially)).

1.3 Since the monoclonal antibodies to human DEC205 are known in the art, the application does not contain a single general inventive concept as required to be present by Article 3(4)(iii) and Rule 13.1 PCT.
When considering the whole set of claims in the light of the description, no further technical features could be identified which could serve as same or corresponding technical features in the sense of Rule 13.2 PCT to restore unity of invention. The fact that antibodies disclosed in the examples contain human germline sequences, cannot provide for a single general inventive concept, since the provision of human antibodies to a known antigen which has been already demonstrated to play a causative role in human pathologies is an activity which does not require inventive skills. When considering the structural features of the antibodies (the germline gene donors, frameworks, CDRs), the ISA is of the opinion that there are no structural features in common between Inventions 1-9 involving different sequences and different combinations of sequences which may represent the technical feature in the sense of Rule 13.2 PCT. In particular, the light chain variable region common for Inventions 2 and 3 is known from D5 and thus cannot serve as the special feature linking these two inventions. Furthermore, it appears that there are no

functional features in common for all or some of the claimed solutions which may serve as the special technical feature in the sense of Rule 13.2 PCT.

1.4 Consequently, the requisite unity of invention (Rule 13.1 PCT) therefore no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the groups of claims.

1.5 As prescribed by Article 17(3) PCT, the invention first mentioned in the claims, ie. Invention 1 has been the subject of the search and this opinion will be consequently given on the subject-matter of Invention 1.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2 Claims 54-82 relate to a subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv)/67.1(iv) PCT. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for in a first or further medical treatment.

3 NOVELTY (Art. 33(2) PCT)

3.1 D1 discloses the sequence of a rat anti DEC205 monoclonal antibody termed NLDC-145 (ATCC Accession No. HB-2990), wherein the VH CDR3 sequence RYFDL falls in the consensus (core) VH CDR3 of the antibodies of the underlying application (compare D1, Figure 3A with Figure 6 of the underlying application). An scFv comprising the VH and VL of the NLDC-145 antibody binds DEC205 on the surface of Langerhans cells and is also expressed as a fusion protein fused to Mycobacterial antigen 85B or ovalbumin for the treatment/prevention of tuberculosis

or ovalbumin overexpressing tumors respectively (pages 40-48).

Therefore, claim 16 is not novel over the disclosure of D1.

D2 discloses the production of a rabbit anti DEC205 serum raised to the entire extracellular domain of human DEC205. Rabbit polyclonal antisera are also produced against the cysteine-rich and fibronectin type II domain and a mouse monoclonal antibody against the carbohydrate domains 1 and 2 of human DEC205 is also generated (page 4758, righthand column, §4-page 4759, lefthand column, §1 and page 4761). Antibodies specific for the extracellular domain of the protein internalize upon binding and thus may serve to load antigens on dendritic cells to treat inter alia cancer and autoimmune diseases (Figures 3-6 and page 4765, righthand column, §3 - lefthand column, § 2).

D3 discloses the production of a murine monoclonal antibody termed MG38 against the cysteine-rich and fibronectin II domain of human DEC205, wherein the antibody does not recognize murine DEC-205 (page 730, righthand column, §2, page 732, righthand column, §2 and Figures 2,4,5 and 6).

D4 discloses monoclonal antibodies raised in mice to two peptides derived from the human DEC205 sequence (residues 1267-1277 and 1227-123), see § 114 and Figure 9.

D5 discloses a fully human antibody termed B11 specific for the mannose receptor on dendritic cells, wherein the light chain variable region is identical to the antibody heavy chain 2F4 of the current application (compare D5, Figures 9 and 14 with Figure 5 of the current application). The antibody was fused to the human chorionic gonadotropin antigen and the conjugate used to stimulate T cell responses (page 34, line 16-page 39, line 17).

D6 discloses the use of the NLDC145 antibody in the prevention or treatment of B16 melanoma tumors overexpressing ovalbumin in mice (page 20, line 15- page 23, line 20).

3.2 In view of the prior art cited, the subject-matter of claims 1-4, 6-15 and 17-84 with respect to Invention 1 appears to be novel

Claim 16 is not novel and therefore the requirements of Art. 33(2) PCT are not met.

4 INVENTIVE STEP (Art. 33(3) PCT)

4.1 D1 is considered to represent the most relevant state of the art. The subject-matter of the Invention 1 differs in that the antibody of the invention contains heavy chain CDR1 and CDR2, and light chain CDR1-3 which differ from the antibody of D1. There is no apparent effect associated with the difference, since both antibodies internalize upon binding to DEC205 on the cell surface and promote T cell stimulation.

4.2 The technical problem to be solved may therefore be defined as to provide a further antibody to human DEC205. The proposed solution is a matter of routine procedures to the person skilled in the art, which in the absence of any surprising or unexpected technical effects, cannot be considered to involve an inventive step. The attention of the applicant is brought to the fact the general provision of human antibodies, which bind a known protein, without any apparent surprising technical effect over the prior art antibodies is not considered to involve an inventive step.

4.3 In view of the above, the present application does not meet the requirements of Article 33(3) PCT, because the subject-matter of Invention 1 does not involve an inventive step.

Re Item VIII

Certain observations on the international application

5 CLARITY (Art.6 PCT)

5.1 Claims 1-3, 83 and 84 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not defined. The claims attempt to define the subject-matter in terms of the result to be achieved. In this instance, however, such a formulation is not allowable because it appears possible to define the subject-matter in more concrete terms, viz. in terms of how the effect is to be achieved by the structural features of the antibody.

5.2 It is not sufficient to characterize an antibody by one of the CDR sequences, since an antibody is structurally made of two light and two heavy chains, both necessary to confer antigen binding specificity. Unless the contrary is shown, it is considered that a CDR is neither equivalent to an antibody, nor sufficient to define the specificity of an antibody. It is not sufficient to characterize an antibody by only one of its variable domain (V_H or V_L) sequences, since the antibody needs at least a V_H and a V_L domain for proper and specific antigen binding.

5.3 Although claims 1-4, 7-9, 14-16, 20, 21, 23-25, 27-29, 34, 83 and 84 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

5.4 The brackets used in claims 1 and 16-20 introduce unclarity since they may imply an optional feature.

5.5 Claim 14 contains a typographical error in item 6 ("viii", probably meant to be "vi") as well as does claim 23 ("d" in item 6, probably meant to be "f" as in claim 27).

Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)

General information	For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.
Amending claims under Art. 19 PCT	Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.
Filing a demand for international preliminary examination	In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT). If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).
Filing informal comments	After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.
End of the international phase	At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPER (international preliminary examination report).
Relevant PCT Rules and more information	Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003